

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/19066

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 20-22 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## PATENT COOPERATION TREATY

PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

09 / 763 559

REC'D 05 JAN 2001

WIPO

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Applicant's or agent's file reference 342342001640	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/19066	International filing date (day/month/year) 18 AUGUST 1999	Priority date (day/month/year) 28 AUGUST 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant ELI LILLY AND COMPANY		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 10 MARCH 2000	Date of completion of this report 17 NOVEMBER 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer CHRISTOPHER LOW
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/19066

**I. Basis of the report****1. With regard to the elements of the international application:\***

- ☒ the international application as originally filed
- ☒ the description:  
pages 1-21, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the claims:  
pages 22-29, as originally filed  
pages NONE, as amended (together with any statement) under Article 19  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the drawings:  
pages NONE, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the sequence listing part of the description:  
pages NONE, as originally filed  
pages NONE, filed with the demand  
pages NONE, filed with the letter of \_\_\_\_\_

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**  
These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

**4. ☒ The amendments have resulted in the cancellation of:**

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

**5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/19066

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement****1. statement**

Novelty (N)	Claims	<u>5-6, 12-13 and 19-22</u>	YES
	Claims	<u>1-4, 7-11 and 14-18</u>	NO
Inventive Step (IS)	Claims	<u>None</u>	YES
	Claims	<u>1-22</u>	NO
Industrial Applicability (IA)	Claims	<u>1-22</u>	YES
	Claims	<u>None</u>	NO

**2. citations and explanations (Rule 70.7)**

Claims 1-4, 7-11 and 14-18 lack novelty under PCT Article 33(2) as being anticipated by WO 97 47645 (MERCK & CO INC). WO 97 47645 discloses cyclohexapeptide compounds and a method for forming a reversible cyclic peptide adduct, comprising adding a 1,2-cis-diol cyclic peptide to an aqueous solution of a boric or boronic acid by adjusting the pH of the solution to a value sufficient for complexation and a pharmaceutical formulation thereof. Thus, the prior art discloses the invention substantially as claimed, and as such, renders claims 1-4, 7-11 and 14-18 as lacking novelty under PCT Article 33(2).

Claims 5-6, 12-13 and 19-22 lack an inventive step under PCT Article 33(3) as being obvious over WO 97 47645 (MERCK & CO INC) in view of Jamison et al and Balkovec et al. The prior art of WO 97 47645, as discussed above as lacking novelty under PCT Article 33(2), discloses the formation of reversible boronate complexes of 1,2-cis-diol cyclic peptide and pharmaceutical composition thereof. The prior art differs from claims 5-6, 12-13 and 19-22 in failing to teach a reversible cyclic peptide adduct having an aminophenyl group and a pharmaceutical formulation thereof, a method for purifying a cyclic peptide having a 1,2-cis-diol moiety and a method for treating a fungal infection by administering the compound thereof. However, the reference of Jamison et al discloses on Figure 1 the use of a reversible cyclic peptide adduct having the structure of aminophenyl group. On pages 240-241, the reference discloses the isolation, purification and *in vitro* and *in vivo* testing of the product for antifungal activity. Similarly, Balkovec et al disclose an aza cyclohexapeptide compounds useful as antifungal agent to treat fungal infections such as mycotic infections in mammals, especially those caused by *Candida* species such as *C. albicans*, *C. tropicalis*, etc. Also, the reference discloses the purification of the cyclic peptide using substantially the same method steps as claimed and the formulation of pharmaceutical composition thereof.

Therefore, the combined teachings of the prior art makes obvious the use of a reversible borate or boronate complexes of 1,2-cis-diol cyclic peptides, method for forming the boronate (Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/19066

**Supplemental B x**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): C07K 7/56, 7/64; A61K 38/00, 38/12; A23J 1/00 and US Cl.: 530/317, 324, 402, 412, 418, 424, 427; 514/2, 9, 11, 12, 639, 664

**V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):**

adduct, method of purifying reversible adduct, pharmaceutical formulation of reversible adduct and method for treating fungal infections thereof.

Claims 1-4, 7-11 and 14-18 meet the criteria as set forth by PCT Article 33(4).

Claims 5-6, 12-13 and 19-22 meet the criteria as set forth by PCT Articles 33(2) and 33(4).

----- **NEW CITATIONS** -----

US 5,378,804 A (BALKOVEC et al) 03 January 1995, see column 3, lines 29-46, column 7, lines 18 to column 8, lines 40, column 13, lines 35 to column 14, lines 45.

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>341342001640</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 99/ 19066</b>	International filing date (day/month/year) <b>18/08/1999</b>	(Earliest) Priority Date (day/month/year) <b>28/08/1998</b>
Applicant <b>ELI LILLY AND COMPANY et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION RELATING TO PRIORITY CLAIM

(PCT Rules 26bis.1 and 26bis.2 and Administrative Instructions, Sections 402 and 409)

From the INTERNATIONAL BUREAU

To:

HAMRE, Curtis, B.  
Merchant & Gould P.C.  
P.O. Box 2903  
Minneapolis, Minnesota 55402-0903  
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 08 June 2001 (08.06.01)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference 12152.75WO01	
International application No. PCT/US99/19016	International filing date (day/month/year) 20 August 1999 (20.08.99)
Applicant PARKER HUGHES INSTITUTE et al	

The applicant is hereby **notified** of the following in respect of the priority claim(s) made in the international application.

1. ☐ **Correction of priority claim.** In accordance with the applicant's notice received on: , the following priority claim has been corrected to read as follows:
  - ☐ even though the indication of the number of the earlier application is missing.
  - ☐ even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:
2. ☐ **Addition of priority claim.** In accordance with the applicant's notice received on: , the following priority claim has been added:
  - ☐ even though the indication of the number of the earlier application is missing.
  - ☐ even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:
3. ☐ As a **result of the correction and/or addition** of (a) priority claim(s) under items 1 and/or 2, the (earliest) priority date is:
4. ☒ **Priority claim considered not to have been made.**
  - ☒ The applicant failed to respond to the Invitation under Rule 26bis.2(a) (Form PCT/IB/316) within the prescribed time limit.
  - ☐ The applicant's notice was received after the expiration of the prescribed time limit under Rule 26bis.1(a).
  - ☐ The applicant's notice failed to correct the priority claim so as to comply with the requirements of Rule 4.

The applicant may, before the technical preparations for international publication have been completed and subject to the payment of a fee, request the International Bureau to publish, together with the international application, information concerning the priority claim. See Rule 26bis.2(c) and the PCT Applicant's Guide, Volume I, Annex B2(IB).
5. ☒ In case where **multiple priorities** have been claimed, the above item(s) relate to the following priority claim:  
US 20 January 1998 (20.01.98) 09/008,898
6. A copy of this notification has been sent to the receiving Office and
  - ☐ to the International Searching Authority (where the international search report has not yet been issued).
  - ☒ the designated Offices (which have already been notified of the receipt of the record copy).

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. (41-22) 740.14.35	Authorized officer  Athina Nickitas-Etienne  Telephone No. (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 05 May 2000 (05.05.00)	
<b>International application No.</b> PCT/US99/19066	<b>Applicant's or agent's file reference</b> 341342001640
<b>International filing date</b> (day/month/year) 18 August 1999 (18.08.99)	<b>Priority date</b> (day/month/year) 28 August 1998 (28.08.98)
<b>Applicant</b> MOSER, Brian, Allen et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

10 March 2000 (10.03.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election
- ☒
- was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer Pascal Piriou</p> <p>Telephone No.: (41-22) 338.83.38</p>
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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 19066

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
**Remark: Although claims 20-22 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.**
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 99/19066

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K7/56 A61K38/12

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 47645 A (MERCK & CO INC ;LEONARD WILLIAM (US); BELYK KEVIN M (US)) 18 December 1997 (1997-12-18) See especially page 6, compound III; reaction schemes I and II; example 1; claim 1 ---	1-4,7-11
A	JAMISON E.A.: "The synthesis and antifungal activity of nitrogen containing hemiaminal ethers of LY303366" JOURNAL OF ANTIBIOTICS., vol. 51, no. 2, February 1998 (1998-02), pages 239-242, XP002126600 JAPAN ANTIBIOTICS RESEARCH ASSOCIATION. TOKYO., JP ISSN: 0021-8820 the whole document --- -/--	1-22



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

23 December 1999

Date of mailing of the international search report

12/01/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Groenendijk, M

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/19066

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 631 364 A (SUNDREHAGEN ERLING ET AL) 20 May 1997 (1997-05-20) the whole document -----	

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/19066

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9747645 A	18-12-1997	AU 3303997 A	07-01-1998
		CZ 9804119 A	12-05-1999
		EP 0912603 A	06-05-1999
		HR 970318 A	31-08-1998
		PL 330400 A	10-05-1999
<hr/>			
US 5631364 A	20-05-1997	US 5702952 A	30-12-1997
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**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
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BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
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BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
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CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
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